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APPLICATION NO.	FILING DATE	FIRST NAMED INVENTOR	ATTORNEY DOCKET NO.	CONFIRMATION NO.
10/849,551	05/20/2004	Jeffrey Moscow	50229-435	7209

7590 06/20/2006

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EXAMINER
BUNNER, BRIDGET E

ART UNIT	PAPER NUMBER
1647	

DATE MAILED: 06/20/2006

Please find below and/or attached an Office communication concerning this application or proceeding.

Office Action Summary	Application No.	Applicant(s)	
	10/849,551	MOSCOW ET AL.	
	Examiner	Art Unit	
	Bridget E. Bunner	1647	

-- The MAILING DATE of this communication appears on the cover sheet with the correspondence address --

Period for Reply

A SHORTENED STATUTORY PERIOD FOR REPLY IS SET TO EXPIRE 3 MONTH(S) OR THIRTY (30) DAYS, WHICHEVER IS LONGER, FROM THE MAILING DATE OF THIS COMMUNICATION.

- Extensions of time may be available under the provisions of 37 CFR 1.136(a). In no event, however, may a reply be timely filed after SIX (6) MONTHS from the mailing date of this communication.
- If NO period for reply is specified above, the maximum statutory period will apply and will expire SIX (6) MONTHS from the mailing date of this communication.
- Failure to reply within the set or extended period for reply will, by statute, cause the application to become ABANDONED (35 U.S.C. § 133). Any reply received by the Office later than three months after the mailing date of this communication, even if timely filed, may reduce any earned patent term adjustment. See 37 CFR 1.704(b).

Status

1)☒ Responsive to communication(s) filed on *07 April 2006*.

2a)☐ This action is **FINAL**. 2b)☒ This action is non-final.

3)☐ Since this application is in condition for allowance except for formal matters, prosecution as to the merits is closed in accordance with the practice under *Ex parte Quayle*, 1935 C.D. 11, 453 O.G. 213.

Disposition of Claims

4)☒ Claim(s) *1-40* is/are pending in the application.

4a) Of the above claim(s) *1-20,23 and 26-40* is/are withdrawn from consideration.

5)☐ Claim(s) _____ is/are allowed.

6)☒ Claim(s) *21,22,24 and 25* is/are rejected.

7)☐ Claim(s) _____ is/are objected to.

8)☒ Claim(s) *1-40* are subject to restriction and/or election requirement.

Application Papers

9)☒ The specification is objected to by the Examiner.

10)☒ The drawing(s) filed on *20 October 2004* is/are: a)☒ accepted or b)☐ objected to by the Examiner.

Applicant may not request that any objection to the drawing(s) be held in abeyance. See 37 CFR 1.85(a).

Replacement drawing sheet(s) including the correction is required if the drawing(s) is objected to. See 37 CFR 1.121(d).

11)☐ The oath or declaration is objected to by the Examiner. Note the attached Office Action or form PTO-152.

Priority under 35 U.S.C. § 119

12)☐ Acknowledgment is made of a claim for foreign priority under 35 U.S.C. § 119(a)-(d) or (f).

a)☐ All b)☐ Some * c)☐ None of:

1.☐ Certified copies of the priority documents have been received.

2.☐ Certified copies of the priority documents have been received in Application No. _____.

3.☐ Copies of the certified copies of the priority documents have been received in this National Stage application from the International Bureau (PCT Rule 17.2(a)).

* See the attached detailed Office action for a list of the certified copies not received.

Attachment(s)

1) ☒ Notice of References Cited (PTO-892)
2) ☐ Notice of Draftsperson's Patent Drawing Review (PTO-948)
3) ☒ Information Disclosure Statement(s) (PTO-1449 or PTO/SB/08) Paper No(s)/Mail Date *12/16/04*.
4) ☐ Interview Summary (PTO-413) Paper No(s)/Mail Date. _____.
5) ☐ Notice of Informal Patent Application (PTO-152)
6) ☐ Other: _____.

DETAILED ACTION

Status of Application, Amendments and/or Claims

The amendment of 20 October 2004 has been entered in full.

Election/Restrictions

Applicant's election of Group V, claims 21-25, drawn to a method of treating a hematological malignancy comprising administering an OCT6 substrate which binds specifically or selectively to the OCT6 protein in the reply filed on 07 April 2006 is acknowledged. Applicant's election of species l (a cytotoxic agent) in the reply filed on 07 April 2006 is also acknowledged. Because applicant did not distinctly and specifically point out the supposed errors in the restriction requirement, the election has been treated as an election without traverse (MPEP § 818.03(a)).

Claims 1-20, 23, and 26-40 withdrawn from further consideration pursuant to 37 CFR 1.142(b) as being drawn to nonelected inventions and species, there being no allowable generic or linking claim. Election was made **without** traverse in the reply filed on 07 April 2006.

Claims 21-22 and 24-25 are under consideration in the instant application.

Sequence Compliance

1. This application contains sequence disclosures that are encompassed by the definitions for nucleotide and/or amino acid sequences set forth in 37 CFR 1.821(a)(1) and (a)(2). However, this application fails to comply with the requirements of 37 CFR 1.821 through 1.825. Specifically, the sequences disclosed in Figures 2A-2F **are not accompanied by the required reference to the relevant sequence identifiers.** Applicant must comply with the requirements of the sequence rules (37 CFR 1.821 - 1.825).

Oath/Declaration

2. The oath or declaration is defective. A new oath or declaration in compliance with 37 CFR 1.67(a) identifying this application by application number and filing date is required. See MPEP §§ 602.01 and 602.02.

The oath or declaration is defective because:

It does not identify the citizenship of each inventor.

Specification

3. The disclosure is objected to because of the following informalities:

3a. The Brief Description of the Drawings for Figure 2 at pg 5 of the specification does not refer to Figures 2A-2F.

3b. The title of the invention is not descriptive. A new title is required that is clearly indicative of the invention to which the claims are directed.

The following title is suggested: "METHOD OF TREATING A HEMATOLOGICAL MALIGNANCY BY ADMINISTERING AN OCT6 SUBSTRATE".

Appropriate correction is required.

Claim Objections

4. Claims 21-22 are objected to because of the following informalities:

4a. Regarding claims 21-22, the acronym "OCT6" should be spelled out in all independent claims for clarity.

4b. Claim 21 is missing a "." after the claim number "21".

Appropriate correction is required.

Claim Rejections - 35 USC § 112

The following is a quotation of the first paragraph of 35 U.S.C. 112:

> The specification shall contain a written description of the invention, and of the manner and process of making and using it, in such full, clear, concise, and exact terms as to enable any person skilled in the art to which it pertains, or with which it is most nearly connected, to make and use the same and shall set forth the best mode contemplated by the inventor of carrying out his invention.

5. Claims 21-22 and 24-25 are rejected under 35 U.S.C. 112, first paragraph, as failing to comply with the enablement requirement. The claim(s) contains subject matter which was not described in the specification in such a way as to enable one skilled in the art to which it pertains, or with which it is most nearly connected, to make and/or use the invention.

The claims are directed to a method of treating a hematological malignancy comprising administering an OCT6 substrate which binds specifically or selectively to the OCT6 transporter protein. The claims recite that the OCT substrate is cytotoxic. The claims also recite a list of hematological malignancies, particularly acute myeloid leukemia.

The specification of the instant application teaches that the OCT6 RNA levels are highest in testis and fetal liver, as well as in peripheral blood leukocytes and bone marrow (pg 14, [50]). The specification discloses that OCT6 RNA expression is enriched in CD34+ cells and leukemia cell lines (pg 14, [5]]; Figure 4). The specification also teaches that high levels of OCT6 RNA expression are observed in peripheral leukemia cells from 25 patients as compared to liver, kidney, and placenta (pg 14, [52]; Figure 5). However, the specification at pg 19 [64-65] and at pg 22 [73-74] only outlines a prophetic procedure for treating a treating a hematological malignancy (leukemias and lymphomas) by administering an OCT6 substrate that is recognized by an OCT6 transporter protein. However, this is not adequate guidance, but is merely an invitation for the artisan to use the current invention as a starting point for further

experimentation. For instance, the prophetic example does not provide guidance as to the identity of any specific OCT6 substrate and does not teach the skilled artisan the optimal dosage, duration, and mode of administration of the OCT6 substrate. The skilled artisan must resort to trial and error experimentation to identity an OCT6 substrate and subsequently determine the optimal dosage, duration, and mode of administration of the OCT6 substrate to treat any hematological malignancy. Such trial and error experimentation is considered undue. According to MPEP § 2164.06, "the guidance and ease in carrying out an assay to achieve the claimed objectives may be an issue to be considered in determining the quantity of experimentation needed." Furthermore, the claimed method may not necessarily treat any hematological malignancy, including acute myeloid leukemia. Relevant literature teaches that treatment of hematological malignancies is unsatisfactory in child and adult patients with acute myeloid leukemia and adult patients with acute lymphocytic leukemia (Hirose et al. J Med Invest 50: 126-135, 2003; abstract, pg 126, 1st paragraph). Voliotis et al. (Sem Oncol 29(No 3, Suppl 8): 30-39, 2002) also disclose that while a cure is possible in some patients with Hodgkins's disease, high-grade non-Hodgkin's lymphoma, acute promyelocytic leukemia, and acute lymphoblastic and myeloid leukemias, the majority of patients with hematologic neoplasia will die from the underlying disease within the first 10 years after diagnosis (pg 30, 1st full paragraph). One skilled in the art would not be able to predict that simply administering an OCT6 substrate would treat any hematological malignancy because cancers result from *multiple* mutations that result in abnormalities in the expression or function of gene products that affect the balance between proliferation, differentiation, and apoptosis (Vogelstein et al. Trends Genetics 9: 138-141, 1993). So, for example, even if an OCT6 substrate was to bind to the OCT6 transporter *in vivo*, a

hematological cancer may not necessarily be treated because other factors can contribute to the pathogenicity of the cancer. Furthermore, a large quantity of experimentation would be required of the skilled artisan to treat all possible leukemias and lymphomas by administration of an OCT6 substrate due to the diverse molecular mechanisms underlying the pathogenicity of the various hematological malignancies (see for example, Tannock and Hill, The Basic Science of Oncology, 1998, McGraw-Hill: New York, pages 53-70, especially pg 55).

Additionally, relevant literature teaches that some cancer cells are intrinsically non-responsive to treatment with anticancer drugs whereas other cancer cells eventually acquire resistance (Tannock and Hill, page 396-410). Hirose et al. disclose that there are several factors that form drug resistance mechanisms against cytotoxic drugs in leukemia cells, such as drug efflux pumps, anti-apoptosis mechanisms, alterations of tumor suppressor genes, altered immunogenicity and membrane structure, drug resistance mechanisms of an individual drug, and clinical risk factors (age, white blood cell count, etc.) (pg 127, 1st full paragraph; Figure 2). Such defense mechanisms of the leukemia cells to the anti-cancer drugs may develop singly or in combinations (top of pg 127). Thus, in view of the observation that many hematological malignancies are recalcitrant to treatment and the plurality of drug resistant mechanisms in hematological malignancies, one skilled in the art would not be able to predict that administering any OCT6 substrate (as required by the claims of the instant application) would treat any hematological malignancy, particularly acute myeloid leukemia.

Due to the large quantity of experimentation necessary to identify an OCT6 substrate and to determine the optimal dosage, duration, and mode of administration of an OCT6 substrate to treat all possible hematological malignancies; the lack of direction/guidance presented in the

specification regarding the same; the absence of working examples directed to the same; the complex nature of the invention; the state of the art which teaches many cancers are drug resistant and that hematological malignancies are recalcitrant to treatment (Hirose et al., Voliotis et al., Tannock and Hill); the unpredictability of administration of any OCT6 to treat a hematological malignancy; and the breadth of the claims which fail to recite limitations as to which OCT6 substrate is to be administered, undue experimentation would be required of the skilled artisan to make and/or use the claimed invention in its full scope.

6. Claims 21-22 and 24-25 are rejected under 35 U.S.C. 112, first paragraph, as failing to comply with the written description requirement. The claim(s) contains subject matter which was not described in the specification in such a way as to reasonably convey to one skilled in the relevant art that the inventor(s), at the time the application was filed, had possession of the claimed invention.

The claims are directed to a method of treating a hematological malignancy comprising administering an OCT6 substrate which binds specifically or selectively to the OCT6 transporter protein. The claims recite that the OCT substrate is cytotoxic. The claims also recite a list of hematological malignancies, particularly acute myeloid leukemia.

The specification of the instant application teaches that "the term 'substrate' refers to a substance, compound, agent, antibody or derivatives and/or fragment thereof, acted upon by the OCT6 transporter protein (e.g., a substance that is taken across the cellular membrane by action of the OCT6 transporter protein)" (pg 11, [46]). However, to provide adequate written description and evidence of possession of a claimed genus, the specification must provide

sufficient distinguishing identifying characteristics of the genus. The factors to be considered include disclosure of compete or partial structure, physical and/or chemical properties, functional characteristics, structure/function correlation, methods of making the claimed product, or any combination thereof. In this case, there is not even identification of any particular structure or function that must be conserved. Dependent claim 22 only requires that the substrate is cytotoxic. Accordingly, in the absence of sufficient recitation of distinguishing identifying characteristics, the specification does not provide adequate written description of the claimed genus of methods of using OCT6 substrates.

Vas-Cath Inc. v. Mahurkar, 19USPQ2d 1111, clearly states that "applicant must convey with reasonable clarity to those skilled in the art that, as of the filing date sought, he or she was in possession *of the invention*. The invention is, for purposes of the 'written description' inquiry, *whatever is now claimed"* (See page 1117). The specification does not "clearly allow persons of ordinary skill in the art to recognize that [he or she] invented what is claimed" (See *Vas-Cath* at page 1116).

The skilled artisan cannot envision the detailed chemical structure of the OCT6 substrates of the encompassed method, and therefore conception is not achieved until reduction to practice has occurred, regardless of the complexity or simplicity of the method of isolation. Adequate written description requires more than a mere statement that it is part of the invention and reference to a potential method of isolating it. The OCT6 substrate itself is required. See *Fiers v. Revel*, 25 USPQ2d 1601 at 1606 (CAFC 1993) and *Amgen Inc. v. Chugai Pharmaceutical Co. Ltd.*, 18 USPQ2d 1016.

One cannot describe what one has not conceived. See *Fiddes v. Baird*, 30 USPQ2d 1481 at 1483. In *Fiddes*, claims directed to mammalian FGF's were found to be unpatentable due to lack of written description for that broad class. The specification provided only the bovine sequence.

Therefore, only a method of treating a hematological malignancy utilizing a specific OCT6 substrate, but not the full breadth of the claims meets the written description provision of 35 U.S.C. §112, first paragraph. Applicant is reminded that *Vas-Cath* makes clear that the written description provision of 35 U.S.C. §112 is severable from its enablement provision (see page 1115).

35 USC § 112, second paragraph

The following is a quotation of the second paragraph of 35 U.S.C. 112:

> The specification shall conclude with one or more claims particularly pointing out and distinctly claiming the subject matter which the applicant regards as his invention.

7. Claims 21-22 and 24-25 are rejected under 35 U.S.C. 112, second paragraph, as being indefinite for failing to particularly point out and distinctly claim the subject matter which applicant regards as the invention.

8. Claims 21-22 and 24-25 are indefinite because the claims do not have a step that clearly relates back to the preamble. For example, there is no step indicating that a hematological malignancy is treated.

9. Regarding claims 24-25, a broad range or limitation together with a narrow range or limitation that falls within the broad range or limitation (in the same claim) is considered indefinite, since the resulting claim does not clearly set forth the metes and bounds of the patent protection desired. See MPEP § 2173.05(c). Note the explanation given by the Board of Patent

Appeals and Interferences in *Ex parte Wu*, 10 USPQ2d 2031, 2033 (Bd. Pat. App. & Inter. 1989), as to where broad language is followed by "such as" and then narrow language. The Board stated that this can render a claim indefinite by raising a question or doubt as to whether the feature introduced by such language is (a) merely exemplary of the remainder of the claim, and therefore not required, or (b) a required feature of the claims. Note also, for example, the decisions of *Ex parte Steigewald*, 131 USPQ 74 (Bd. App. 1961); *Ex parte Hall*, 83 USPQ 38 (Bd. App. 1948); and *Ex parte Hasche*, 86 USPQ 481 (Bd. App. 1949). In the present instance, claim 24 recites the broad recitation "leukemia", and the claim also recites ALL, AML, acute lymphoid leukemia biphenotypic, AUL, CML, erythroleukemia, granuloxytic leukemia, lymphoma, monocytic leukemia, myeloma, myelomonocytic leukemia, myelodysplastic syndromes, non-Hodgkin lymphoma, and progranulocytic leukemia which is the narrower statement of the range/limitation.

Conclusion

No claims are allowable.

The art made of record and not relied upon is considered pertinent to applicant's disclosure:

Gong et al. Exp Hematol 30 : 1162-1169, 2002 (disclose the OCT6 polypeptide of SEQ ID NO: 2 of the instant application)

Guiseppe et al. Haematologica 86 : 121-127, 2001 (discuss methotrexate and its role in leukemias)

Koepsell et al. Eur J Physiol 447 : 666-676, 2004 (Review of the SLC22 transporter family)

Koepsell et al. Rev Physiol Biochem Pharmacol 159 : 36-90, 2003 (review of organic cation transporters)

Any inquiry concerning this communication or earlier communications from the examiner should be directed to Bridget E. Bunner whose telephone number is (571) 272-0881. The examiner can normally be reached on 8:30-4:30 M-F.

If attempts to reach the examiner by telephone are unsuccessful, the examiner's supervisor, Brenda Brumback can be reached on (571) 272-0961. The fax phone number for the organization where this application or proceeding is assigned is 571-273-8300.

Information regarding the status of an application may be obtained from the Patent Application Information Retrieval (PAIR) system. Status information for published applications may be obtained from either Private PAIR or Public PAIR. Status information for unpublished applications is available through Private PAIR only. For more information about the PAIR system, see http://pair-direct.uspto.gov. Should you have questions on access to the Private PAIR system, contact the Electronic Business Center (EBC) at 866-217-9197 (toll-free). If you would like assistance from a USPTO Customer Service Representative or access to the automated information system, call 800-786-9199 (IN USA OR CANADA) or 571-272-1000.

BEB
Art Unit 1647
02 June 2006

Bridget E. Bunner

BRIDGET BUNNER
PATENT EXAMINER